

**Remarks/Arguments:**

***Summary of Changes Made***

By this Amendment, claim 16 has been amended, claim 20 has been canceled and new claims 21-37 have been added to the application. Thus claims 1-19 and 21-37 are pending in the application.

Claim 16 has been amended to specify that the polymer, lipid and/or excipient is dissolved in the second solvent, rather than the first solvent, and that the precipitated particles collected in the collecting step have a core comprising the first solute and a shell comprising the polymer, lipid and/or excipient, as disclosed in paragraph [0059] of the application. Claim 16 has also been amended to correct a minor typographical error. The subject matter of new claims 21-37 is disclosed in paragraphs [0054] through [0060] of the application. No new matter has been added to the application.

***Claim Rejections - 35 USC § 102***

In the prior Office Action, the Examiner rejected claim 20 under 35 U.S.C. §102(b) and/or (e) as being anticipated by Holl et al., U.S. Pat. No. 6,471,392, Zhou et al., U.S. Published App. No. 2004/0115123 and Johnson et al., U.S. Published App. No. 2004/0091546. By this Amendment, claim 20 has been canceled, without prejudice, thereby rendering the prior rejection thereof moot. Applicants reserve the right to pursue the subject matter of canceled claim 20 in one or more divisional applications.

Also in the prior Office Action, the Examiner rejected claims 1-19 under 35 U.S.C. §102(e) as being anticipated by Johnson et al. Beginning on page 2 of the Office Action, the Examiner contends that:

"Johnson et al. disclose providing a 1<sup>st</sup> solution with dissolved solute (page 3, paragraph 34, providing anti-solvent that may be supercritical carbon dioxide (page 6, paragraph 58 and, if necessary, page 7, paragraph 63), flowing the fluids through a chamber of vessel containing a rotor to mix (page 4, paragraph 41) and mixing in the annular space between wall of vessel and rotor and collecting precipitated nanoparticles (paragraphs 41 and 58)."

Applicants respectfully disagree with the Examiner's characterization of the teachings of Johnson et al.

The Johnson et al. disclose a process whereby a solution comprising one or more amphiphilic copolymers dissolved in a process solvent is rapidly mixed with a non-process solvent to flash precipitate nanoparticles of the amphiphilic copolymers in the resulting solution (see page 3, paragraph [0034]). Amphiphilic copolymers are broadly defined by Johnson et al. as being comprised of subunits or monomers that have different hydrophilic and hydrophobic characteristics (see page 5, paragraph [0050]). Preferred amphiphilic copolymers are described as diblock or triblock compositions containing at least one of the following: a polystyrene block, a polyethylene oxide block, a polybutylacrylate, a polyacrylic acid, polybutylmethacrylate block, or a polyethyleneoxide block (see page 6, paragraph [0056]).

Johnson et al. teach that the process solvent must be capable of dissolving at least 0.1% of the copolymer by weight and is typically a liquid at room temperature (see page 6, paragraph [0057]). Johnson et al. further teach that the process solvent can be a mixture of solvents or an organic solvent (see page 6, paragraph [0057]). But, in a more preferred embodiment of the invention, Johnson et al. teach that the process solvent is an alcohol such as methanol or an ether such as tetrahydrofuran (see page 6, paragraph [0057]).

Johnson et al. further teach that the non-process solvent must be capable of changing the local molecular environment of the copolymer and cause local precipitation of either the hydrophobic or hydrophilic blocks (see page 7, paragraph [0063]). Johnson et al. teach that the non-process solvent can be water or an aqueous solution containing a buffering agent, salt, colloid dispersant, or inert molecule, or could be a mixture of solvents such as alcohol and water (see page 7, paragraph [0063]).

On page 6, at paragraph [0058], Johnson et al. teach that:

"In another embodiment of the invention, the process or non-process solvent may consist of a liquefied gas. In this embodiment, the process or non-process solvents are a gas at room temperature but are put in liquid form for the process by changing the pressure or temperature or both in the mixing vessel or inlet tubes. An example of a liquefied gas used as a non-process solvent is carbon dioxide under adequate pressure with or without a modifier, such as ethanol. After mixing, a post processing step consisting of a pressure or temperature change or a change in both is made and the solvent evaporates leaving the nanoparticles."

The Examiner contends that in the quote paragraph, Johnson et al. teach that the non-process solvent (described as an "anti-solvent" by the Examiner) may be supercritical carbon

dioxide. Applicants respectfully disagree. In the quoted paragraph, Johnson et al. suggest that liquid carbon dioxide may be used as a process solvent or a non-process solvent, but Johnson et al. clearly do not ever disclose, teach or suggest that supercritical carbon dioxide can be used for such purposes. It should be noted that carbon dioxide can only exist in a supercritical state at high pressure and at temperatures above 31°C (i.e., greater than about 88°F), which is above the typical or normal "room temperature" of about 72~75°F.

The Examiner also refers to page 7, paragraph [0063] of Johnson et al. as supporting the contention that supercritical carbon dioxide is contemplated for use in the invention. Applicants respectfully submit that the Examiner is in error. At page 7, paragraph [0063], Johnson et al. teach in pertinent part that:

"The final solvent containing the nanoparticles (sic) can be altered by a number of post treatment processes, such as but not limited to dialysis, distillation, wiped film evaporation, centrifugation, lyophilization, filtration, sterile filtration, extraction, supercritical fluid extraction, or spray drying. The processes typically occur after the nanoparticle formation but could also occur during the nanoparticle formation process."

The teachings set forth in paragraph [0063] very clearly relate to "post treatment processes" for altering the "final solvent containing the nanoparticles". Each of the processes mentioned by Johnson et al. is a process that can be used to separate the already-formed nanoparticles from the resulting final solvent. These processes are not alternative embodiments of the basic invention disclosed by Johnson et al., which results in the production of a "final solvent containing the nanoparticles".

Johnson et al. clearly mention "supercritical fluid extraction" only in the context of being one of the post treatment process that can be used to alter the final solvent containing the nanoparticles. Although no explanation whatsoever is provided by Johnson et al. regarding what is intended by the phrase "supercritical fluid extraction", one can only reasonably conclude that the phrase refers to the extraction of one or more of the process and/or non-process solvents from the final solvent containing the nanoparticles. No other reasonable conclusion can be drawn. Thus, the only reference in Johnson et al. to supercritical fluid is in the context of supercritical fluid extraction, which refers to a post- treatment nanoparticle separation process, not a particle precipitation process as claimed in the present invention.

It is well settled that a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). In this instance, Johnson et al. clearly do not teach precipitating nanoparticles into a mixture comprising supercritical fluid. Accordingly, Johnson et al. do not anticipate claim 1 of the present application. Claims 2-19 depend from claim 1 and are thus patentable over Johnson et al. for the reasons that claim 1 is patentable over such reference.

### ***Claim Rejections - 35 U.S.C. § 103***

In the prior Office Action, the Examiner rejected claims 1-19 under 35 U.S.C. §103(a) as being unpatentable over Saim et al., U.S. Published App. No. 2003/0066800, in view of Holl et al. and Zhou et al. Saim et al. discloses two methods of precipitating small particles onto a carrier material. In one method (which is referred to as "Mode 2" in Saim et al.), a solute that has been dissolved in a liquid solvent to form a solution is precipitated into a supercritical fluid having a carrier powder material dispersed therein. The solute precipitates from the liquid solvent solution onto the carrier powder material or, subsequent to precipitation into the supercritical fluid, collides with and becomes adhered to or bonded to the carrier powder material to form a composite particle. Although the method disclosed in Saim et al. does involve the formation of particles via precipitation of a solute from a liquid solution into a supercritical fluid, the method differs substantially from the method claimed in the present application.

Claim 1 of the present application requires that the first solution comprising the first solute dissolved or dispersed in the first solvent be dispensed into a mixing zone that is defined as being the space between the inner wall of the chamber and the adjacent surface of the rotating rotor disposed within the chamber. In contrast to claim 1, Saim et al. teach that the liquid solution "is preferably introduced into the vessel from a level below or slightly above the upper surface of the carrier powder bed at rest." (see page 7, paragraph [0085]). Figure 1 of Saim et al., which includes a simplified flow diagram showing Mode 2 of the invention, shows the liquid solution being dispensed well above the blades of the rotor, and certainly not in a mixing zone "defined as a space between an inner wall of the chamber and an adjacent surface of the rotating rotor" as claimed.

The other two references cited and relied upon by the Examiner cannot properly be combined with Saim et al. to read on claim 1 of the present invention. Holl et al. discloses an

apparatus for processing materials that includes two cylindrical apparatus members mounted for rotation relative to one another. Reactants are pumped into contact with each other in the space between the smooth facing surfaces of the cylindrical apparatus members. Holl et al., however, does not teach that the apparatus is suitable for use in supercritical fluid processing. Moreover, Holl et al. cannot be combined with Saim et al. because the latter teaches that the liquid solution "is preferably introduced into the vessel from a level below or slightly above the upper surface of the carrier powder bed at rest." (see page 7, paragraph [0085]), and not into the space between smooth facing surfaces of cylindrical apparatus members as in the former.

The second applied reference, Zhou et al., discloses a method for producing nanometer grade powders by providing an A reactant solution and a B reactant solution that can rapidly react with each other to form a precipitate, continuously adding A and B reactant solutions into a mixing reacting precipitator with a stator and a rotor and then post treating the precipitate-containing slurry to obtain the particles. Zhou et al., however, do not contemplate that the A reactant solution and/or the B reactant solution can be or comprise a supercritical fluid. It should be noted that in paragraph [0043] of the specification, Zhou et al. mention that the resulting nanometer grade powders can be recovered by a "supercritical drying" post-treatment step, which shows that while Zhou et al. clearly knew of supercritical fluid processing techniques, they never contemplated that supercritical fluid could be used as part of the A reactant solution and/or the B reactant solution. Clearly, the teachings of Zhou et al. cannot properly be combined with Saim et al., which does involve the precipitation of particles into a supercritical fluid.

It has often been said that if an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed.Cir. 1988). Claim 1 is not obvious in view of the teachings of Saim et al., Johnson et al., Holl et al. and/or Zhou et al., alone or in combination. Accordingly, dependent claims 2-19 are also not obvious in view of such references.

New claims 21-37 relate to the embodiment of the invention described in paragraphs [0054] to [0060] of the application. None of the cited references, alone or in combination, fairly disclose, teach or suggest dispensing a first solution and a second solution into a supercritical fluid filled vessel in a mixing zone to form a precipitate having a core comprising the solute of the first solution and a shell comprising the solute of the second solution. Johnson et al. do not contemplate supercritical fluid processing. Saim et al. precipitate a material onto an existing

powder, rather than precipitating a core material that acts as a seed for a precipitated shell. And Holl et al. and Zhou et al. do not teach the formation of core-shell type particles. Claims 21-37 are clearly patentable over the cited prior art.

**Conclusion**

In view of the foregoing, claims 1-19 and 21-37 are believed to be in condition for allowance. The issuance of a timely Notice of Allowance is therefore respectfully requested.

Respectfully submitted,

RANKIN, HILL, PORTER & CLARK, L.L.P.

A handwritten signature in black ink, appearing to read "Randolph E. Digges, III", is written over a horizontal line.

Randolph E. Digges, III  
Reg. No. 40,590

925 Euclid Avenue  
Suite 700  
Cleveland, Ohio 44115-1405  
(216) 566-9700